Analysis of the Role of Bhlhb5 and Prdm8 in Neural Development

Abstract

Two transcription factors, Bhlhb5 and Prdm8, have been linked together in neural development through the discovery that Bhlhb5 and Prdm8 knockout mice exhibit the same behavioral phenotypes (i.e. the development of skin lesions and a handstand posture). In my thesis, I hypothesized that Bhlhb5 and Prdm8 may have a cooperative role in the same regulatory processes underlying neuronal differentiation and maturation. I proposed three models of interaction between Bhlhb5 and Prdm8, and conducted immnoprecipitation analysis to determine which model was best supported by the data. The three models were: 1) Bhlhb5 and Prdm8 regulate the same target genes, but do not bind together in complex, 2) Bhlhb5 and Prdm8 interact in complex to regulate the same gene targets, and 3) Prdm8 and Bhlhb5 each regulate the transcription of unique proteins that are critical mediators of a common pathway. To address my hypothesis that Bhlhb5 and Prdm8 are crucial in the same neurons in development, I examined via immunohistochemistry techniques their protein expression patterns in the mouse brain and spinal cord.

Results from my thesis provided evidence in support of the models where Bhlhb5 and Prdm8 do not bind directly together in complex. Moreover, my analysis determined that Prdm8- expressing neurons are significantly lost in the spinal cord of Bhlhb5 mutants, that high levels of Bhlhb5 and Prdm8 co-expression are observed in the brain and spinal cord, and that Prdm8 mutants exhibit loss of the corticospinal tract. These results all contributed towards my overarching hypothesis that Bhlhb5 and Prdm8 are crucial regulators of a common pathway that underlies neuronal development in the mammalian central nervous system.